## Synopsis of LYMERixÒ Phase 4 Observational Study

Background: Rare but significant adverse events associated with use of a product may not be recognized in studies of the sizes typical of pre-licensure studies. This post-marketing study will monitor subjects immunized with LYMErix® for the development of Lyme disease, selected musculoskeletal and neurologic disorders, and selected adverse events potentially related to vaccination, hospitalization and death.

Design: Prospective cohort study

Enrollment: 25,000 adults receiving at least one dose of LYMErix®
75,000 age- and sex-matched unvaccinated (with LYMErix®) individuals according to HMO data

Site: Harvard Pilgrim Health Care (HMO) in New England.

Enrollment: 2 years
Follow-up: 4 years from date of vaccination

Objectives

Evaluation of whether exposure to LYMErix® is a risk factor for:

- New onset inflammatory arthropathy (primary endpoint)
- Lyme disease (LD)
- Treatment resistant LD
- Rheumatoid arthritis
- Certain neurologic diseases (MS, GBS, acute disseminated encephalomyelitis, transverse myelitis, cranial neuritis, mononeuritis multiplex, myasthenia gravis, syringomyelia)
- Allergic events
- Hospitalizations
- Death

Methods: Clinical events of interest will be identified using ICD-9 coding for ambulatory and in-patient claims data. Selected outcomes will be confirmed by blinded review of the full medical record by an appropriate subspecialist. Established diagnostic criteria will be used where applicable. The incidence of predefined adverse events in the exposed cohort will be compared to the incidence of adverse events in the unexposed cohort matched by age, sex, and practice affiliation.

Results
(to date): As of November 6, 2000, a total of 2,568 vaccine recipients and 7,497 matched unvaccinated individuals have been enrolled. This represents approximately 10% of the planned total enrollment and 50% of the

number in the vaccine arm of the phase 3 clinical trial. Incident cases of selected rheumatologic diagnostic codes have been identified. While no obvious patterns are present in this data suggesting higher incidence of rheumatological conditions among vaccinees than among non-vaccinees, the current analysis of data and the small number of vaccinees in the study do not allow firm conclusions to be drawn from the study. In addition, the sponsor has not presented incident data and analysis on other study endpoints.